Long-term insulin sensitivity and beta-cell function in short children born SGA treated with GH and GnRHa: Results of a randomized, dose-response trial

Manouk van der Steen[1,2], Annemieke J. Lem[1], Danielle C.M. van der Kaay[1], Anita C.S. Hokken-Koelega[1,2]
[1] Dutch Growth Research Foundation, Rotterdam [2] Erasmus University Medical Center Rotterdam/Sophia Children's Hospital, Dept. of Pediatrics, Subdivision Endocrinology, Rotterdam, The Netherlands
m.vandersteen@kindengroei.nl

CONCLUSIONS

- Combined GH/GnRHa treatment has no long-term negative effects on insulin sensitivity and β-cell function in young adults compared to only GH
- Started in early puberty, a GH dose of 2mg/m²/day results in a similar insulin sensitivity and β-cell function at AH as GH 1mg/m²/day

Background

Children born SGA can benefit from combined treatment of GH and 2 years of GnRH analogue (GH/GnRHa). GnRHa treatment might have negative effects on insulin sensitivity. Long-term effects of combined GH/GnRHa treatment and GH-dose effects on insulin sensitivity and β-cell function at adult height (AH) are unknown.

Aims

I. To investigate insulin sensitivity and β-cell function during GH treatment, with or without 2 years of additional GnRHa.
II. To assess whether a higher GH dose results in a similar insulin sensitivity and β-cell function at AH.

Results

I. At AH, insulin sensitivity and β-cell function were similar between children treated with combined GH/GnRHa and those treated with GH only
II. A higher GH dose of 2mg/m²/day resulted in a similar insulin sensitivity and β-cell function as GH 1mg/m²/day

I. Insulin sensitivity and β-cell function at AH

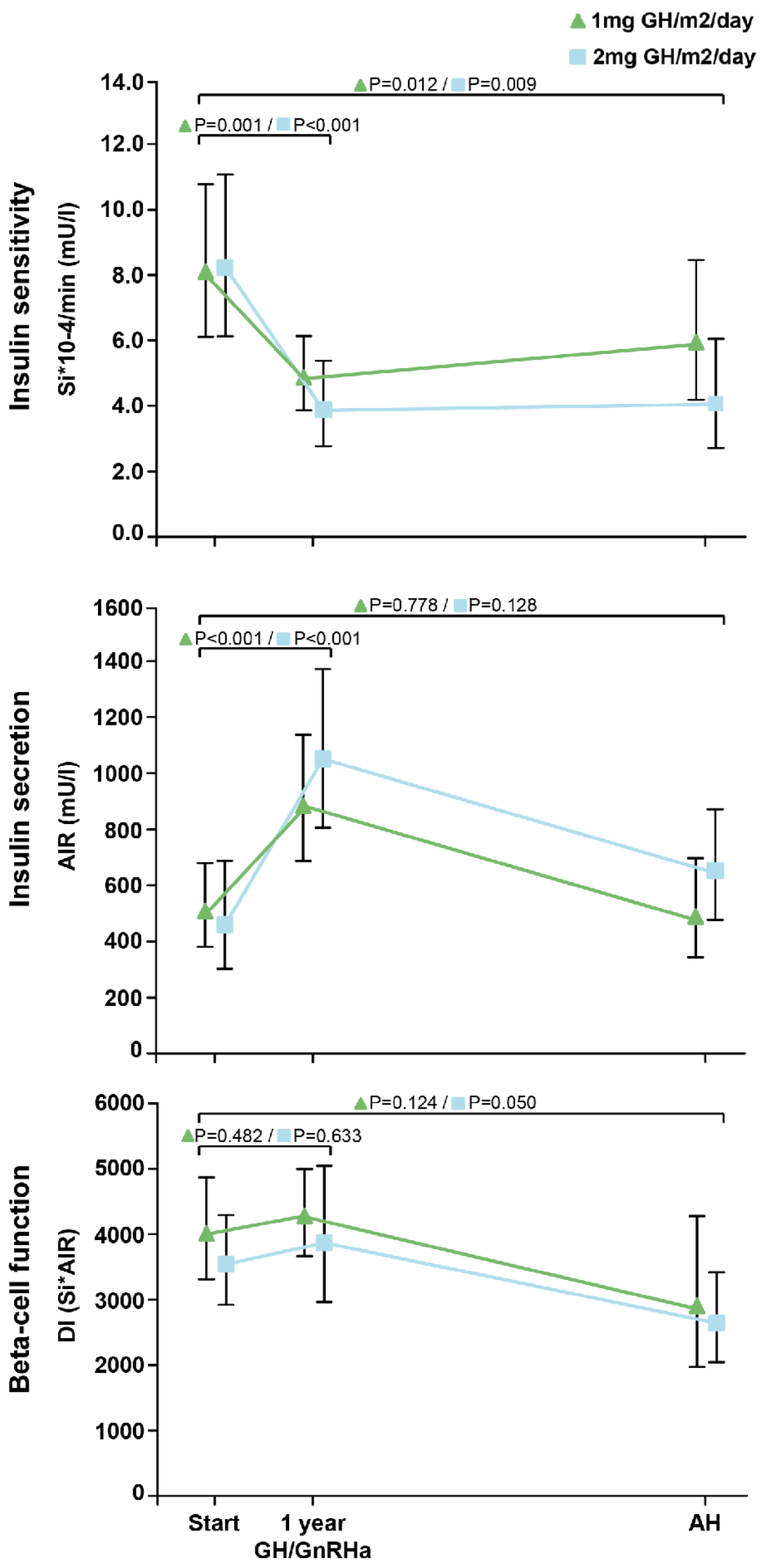
	Total group	GH/GnRHa	GH	P
N	76	48	28	
Age	17.4 (1.2)	17.4 (1.1)	17.4 (1.3)	0.853
Si x 10^{-4}/min (mU/l)	6.1 (5.2)	6.8 (5.8)	5.0 (3.9)	0.176
AIR (mU/l)	706.9 (564.4)	726.3 (616.7)	673.8 (470.2)	0.881
DI (Si x AIR)	2929.3 (1762.9)	3159.4 (1871.4)	2534.7 (1510.2)	0.066
Fasting glucose (mmol/l)	5.0 (0.5)	5.0 (0.5)	5.1 (0.6)	0.506
Fasting insulin (mU/l)	13.6 (6.6)	13.6 (7.3)	13.7 (5.2)	0.752

Methods

- 110 short SGA children, 11.4 years at start (59 girls)
- GH treatment until AH, mean follow-up 5.9 years
- At start of puberty
  Height < 140cm → additional GnRHa for 2 yrs
  - GH/GnRHa-group: N=67 / GH-group: N=43

  Randomisation to GH **1mg/m²/day** (~0.033mg/kg/d) or **2mg/m²/day** (~0.067mg/kg/d)

II. GH-dose effect on insulin sensitivity and β-cell function in children with GH/GnRHa



FSIGT

Frequently Sampled Intravenous Glucose Tolerance (FSIGT) test to measure insulin sensitivity (Si), acute insulin response (AIR) and beta-cell function (disposition index, DI)

This study was an investigator initiated study, supported by an independent research grant from Pfizer